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Richard Denison
<rdenison@environmentaldefense.org>
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To: NCIC OPPT@EPA, ChemRTK HPV@EPA, Rtk Chem@EPA, NCIC HPV@EPA, Karen Boswell/DC/USEPA/US@EPA, Edwin.L.Mongan-1@usa.dupont.com
cc: MTC@mchsi.com, GEORGE LUCIER <lucierg@msn.com>, Karen Florini <KFlorini@environmentaldefense.org>, Richard Denison <RDenison@environmentaldefense.org>
bcc:
Subject: Environmental Defense comments on the Aminoalkylnitriles Category

(Submitted via Internet 1/7/05 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, / boswell.karen@epa.gov, chem.rtk@epa.gov, MTC@mchsi.com, and Edwin.L.Mongan-1@usa.dupont.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for the **Aminoalkylnitriles Category**.

E. I. Du Pont de Nemours & Company, in response to the EPA HPV Challenge, has submitted robust summaries and a test plan for two chemicals: propanenitrile, 2-amino-2-methyl- (PAM, CAS# 19355-69-2) and butanenitrile, 2-amino-2-methyl- (BAM, CAS# 4475-95-0), and DuPont has proposed that they be considered together as a category. DuPont has also submitted data for 2,2'-azobis-(2-methylbutyronitrile) (BADM, CAS# 13472-08-7), previously reviewed under the HPV Challenge, with the proposal that data developed for that chemical be bridged to predict the fate and toxicity of the chemicals in the proposed category.

After reviewing this submission and the data therein, we agree that -- given the close structural similarity of these chemicals and the fact that they are used in similar applications -- it is appropriate that they be considered a chemical category. We also agree that BADM can be used as surrogate for some -- but not all -- SIDS endpoints.

The test plan also provides a brief description of the production, use and transport of these chemicals. The sponsor claims that members of the proposed category are produced solely by DuPont as site-limited intermediates and used exclusively for the synthesis of the corresponding azonitriles at another DuPont facility. The sponsor provides some information on the manufacturing process and worker safety practices and some on-site monitoring data. According to the test plan, these chemicals are produced in closed systems, transferred to tank trucks through closed lines and transported to their site of use, with precautions in place for safe handling and use. The monitoring data indicate air levels of approximately 1 ppm at the manufacturing facility. No information was provided, however, on whether or not BAM and PAM are present in the azonitriles or other products that are synthesized using the aminoalkylnitriles. Based on this lack of information and the detection of the chemicals in the workplace evident from the monitoring data, we do not agree that the aminoalkylnitriles can be considered site-limited intermediates.

It appears the major source of concern for environmental and human exposure would be a release of these highly toxic chemicals in the course of an accident in transport. Thus, it would be of interest to have additional information regarding measures that would be taken in case of such a release.

Our review of this submission indicates that it is complete and well-organized to present the available data for each chemical in the category and, where necessary, to bridge data developed for 2,2'-azobis-(2-methylbutyronitrile) to predict properties of the members of this category. The sponsor proposes to conduct developmental toxicity and in vivo genetic toxicity tests on BAM, as adequate data do not exist for these endpoints. While we agree with this proposal, we do not agree that no other additional studies are needed. Specifically, evaluation of the data presented in the robust summary for the dermal repeat dose study on BADM indicates it is not suitable to serve as an adequate surrogate for this endpoint, and we also recommend that the sponsor conduct an algal toxicity study.

In regard to the dermal repeat dose study, we note that it was conducted in rats and that there was no evidence of toxicity, indicating that the BADM was not absorbed into the systemic circulation. In fact, the sponsor argues that the NOEL should be 30 mg/kg, the highest dose tested. However, given that the aminoalkylnitriles are highly toxic to rats following oral or inhalation doses, the dermal route is inappropriate for use in meeting requirements for the repeat dose endpoint. Since the sponsor is already planning on conducting a developmental toxicity study, we recommend that a combined repeat dose/reproductive/ developmental toxicity study be conducted on one of the two category members using the oral or inhalation route of exposure. The reproductive component is needed because the aminoalkylnitriles may not be solely site-limited intermediates.

We also recommend that the sponsor conduct an algal toxicity test on either PAM or BAM. The reason for this recommendation is that the aminoalkylnitriles are very toxic to fish and moderately toxic to aquatic invertebrates. The values presented in Table 4 of the test plan indicate that ECOSAR estimates dramatically underestimate the actual ecotoxicity of category members. This underestimation is by three orders of magnitude for BAM in fish, and by 40-fold for BADM in algae. Since no experimental data exist for either PAM or BAM for algal toxicity, at least one of these substances needs to tested for this endpoint. Furthermore, BADM data for algal toxicity may not be appropriate for use since BADM is not biodegradable, whereas PAM and BAM are readily biodegraded.

Other comments:

1. The test plan mentions that these chemicals decompose when heated. It should also be mentioned that one of the products of their decomposition is hydrogen cyanide. This could be very important information in case of an accident.
2. The human exposure section of the test plan indicates that the DuPont AEL as an 8- or 12-hour time weighted average is 500 ppm. This cannot be true since PAM is highly toxic, with an LC50 of 71 ppm in rats. We assume that the AEL is 500 ppb, not 500 ppm.

3. It should be stated whether these chemicals are toxic to the bacteria used in the Ames assays. This is relevant because all three chemicals degrade to release cyanide on contact with water, and the toxicity of cyanide could have accounted for the negative results obtained with the bridged chemical, 2,2' -azobis-(2-methylbutyronitrile).
4. Are any data available on metabolism of the aminoalkylnitriles in mammals or aquatic organisms relevant to the toxicity of these chemicals?
5. Some of the studies cited are somewhat dated and were not conducted under GLP, but appear to be adequate to address the relevant SIDS elements.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Hazel B. Matthews, Ph.D.
Consulting Toxicologist, Environmental Defense

Richard Denison, Ph.D.
Senior Scientist, Environmental Defense